REMARKS

Reconsideration of the allowability of the present application in view of the above claim amendments and the following remarks is requested respectfully.

Discussion of the Claims

In his Action, the Examiner acted upon Claims 1 to 8, 16, 20 to 22, 26, and 29 of the application, Claims 9 to 15, 17 to 19, 23 to 25, 27, 28, and 30 to 52 having been withdrawn previously from further consideration as being directed to non-elected species. This withdrawal is subject to being rescinded should claims generic to the non-elected species be found allowable. MPEP §809.02(c).

Claims 1, 2, 17, 18, 22, 30, and 42 have been amended. No claims have been cancelled or added.

The claims pending presently are Claims 1 to 52.

Discussion of the Amendments

Claims 1 and 30 have been amended to define the single-chain polypeptide as having at least one domain which is a variable heavy chain domain or a variable light chain domain of a sFv polypeptide. Support for this amendment is found in the application at pages 8 to 13.

Claim 22 has been amended to clarify that the nucleic acid recited therein comprises a therapeutic gene.

Amendments have been made to Claims 17 and 18 for the purpose of better clarifying the present invention. Support for this amendment is in the application at, for example, page 15, lines 20 to 24.

Amendments of an editorial nature has been made to Claims 2 and 42.

No new matter has been added.

Discussion of the Examiner's Section 102(b) Rejection

The Examiner has rejected independent Claim 1 and related dependent Claims 3 and 4 as being anticipated by Wagner et al., *PNAS USA*, 87: 3410-3414 (1990). This rejection is traversed.

Claim 1 defines the compound as comprising an effector segment which comprises a cysteinyl residue that is involved in the coupling of the single-chain binding polypeptide with the nucleic acid binding moiety. Wagner et al. does not disclose such an effector segment. In fact, the coupling of transferrin with the nucleic acid binding moiety is achieved though a different means in Wagner et al. The nucleic acid binding moiety therein is modified with 3-mercaptopropionate and transferrin is modified with 3-(2-pyridylthio)propionate. A disulfide bond is then formed using these added groups. Nowhere in Wagner et al. is there a disclosure of the use of a cysteinyl residue in the coupling of the single-chain binding polypeptide with the nucleic acid binding moiety. The Examiner's rejection is, therefore, in error.

In addition to the aforementioned, applicants advise also that the claims now define the single-chain binding polypeptide as being one which comprises a domain of a sFv polypeptide. Wagner et al. does not disclose such a polypeptide.

Discussion of the Examiner's Section 103 Rejection

The Examiner rejected Claims 1 to 8, 16, 20 to 22, 26, and 29 as being unpatentable over the disclosure of the aforementioned Wagner et al. publication in view of U.S. Patent No. 5,977,322 to Marks et al., and International Application Publication No. WO 00/04922 to Konadu et al.

To establish a *prima facie* case of obviousness, the Examiner must show that each defining recitation of the involved claim is taught or suggested by the cited references. MPEP § 2143. Such must be found either in the references themselves or in the knowledge generally available to one skilled in the art. Applicants submit respectfully that this has not been shown.

Each of the independent claims (Claims 1 and 30) recites that the gene-delivery compound comprises an effector segment which includes a cysteinyl residue which couples with a nucleic acid-binding moiety. As stated above, Wagner et al. does not disclose the use of such an effector segment. Further, none of the other cited art teaches or suggests such an effector segment and the Examiner has not even argued that they do.

Given that not all defining recitations of the claims are taught or suggested by the cited references, the Examiner has not established a *prima facie* case of obviousness. The Examiner's rejection is, therefore, in error.

Discussion of the Examiner's Rejection
Under the Written Description Requirement of Section 112, First Paragraph

The Examiner rejected Claims 4 and 5 under the written description requirement of Section 112, first paragraph, because he considered the claims to encompass the use of any single-chain polypeptide which can bind to any surface marker of a mammalian cell. The Examiner's rejection is based on his view that there is not adequate support in the application for all single-chain binding polypeptides.

It is submitted that the Examiner's rejection has been overcome by the amendment to independent Claim 1, on which Claims 4 and 5 are dependent. As stated above, the amendment further defines the single-chain binding polypeptide as having a domain of an sFv polypeptide. These structures are described in the application at page 8, lines 17 to 27, and page 9, lines 1 to 28, and page 10, lines 1 to 8.

The Examiner states that factors to be considered in determining whether the written description requirement is met are whether there exists a description of: (A) a structure or a partial structure for the invention; (B) physical or chemical properties of the invention; (C) functional characteristics of the invention; (D) correlation between the structure and the functional characteristics; or (E) methods for making the claimed invention. Applicants submit that the application contains an adequate description of all five of these elements.

The structure of the polypeptide is discussed above.

Regarding the physical properties of the invention, it is known that, through an assay, one skilled in the art may determine which relevant domains of the single-chain binding polypeptides will bind to which cell-surface markers (see page 10, lines 9 to 19, of the application). A description of exemplary markers appears in the application at page 12, lines 17 to 29, and page 13, lines 1 to 6.

The functional characteristic of the polypeptide is that it binds a cell surface marker (see, for example, page 1, lines 7 to 12, of the application). The relationship of this functional characteristic of the polypeptide to the structure thereof is that the variable heavy chain and the variable light chain of the polypeptide form the site at which the polypeptide binds to the cell surface marker (see page 9, lines 3 to 14, of the application).

Respecting methods for making the invention, a method for making a combination of the single-chain binding polypeptide and an effector segment containing the cysteine is adequately described in Example 1. A method for making a combination of the single-chain binding polypeptide and additional effector segements is described in Example 2. One skilled in the art would recognize these as general methods which are applicable regardless of the various elements (e.g., type of nucleic acid binding moiety, type of single-chain binding polypeptide) used.

Given the above, it is abundantly clear that applicants have adequately described the invention and it is abundantly clear that applicants were in possession of the invention as claimed. Accordingly, it is requested that the Examiner's rejection be withdrawn.

Discussion of the Examiner's Rejection
Under the Enablement Requirement of Section 112, First Paragraph

The Examiner rejected Claims 1 to 8, 16, 20 to 22, and 29 under the enablement requirement of Section 112, first paragraph. The Examiner considers the claims to be drawn to a compound which comprises the C6ML3-9 sFv' SP conjugate and has asserted that applicants have not enabled the use of such a compound in the delivery of a nucleic acid to any cell since not all cells express the erbB2 antigen which is bound by the conjugate. The Examiner has asserted also that the application enables only the use of this compound to deliver a nucleic acid to cells *in vitro* and not *in vivo*.

The Examiner appears to base his rejection on his belief that the above conjugate can only bind erbB2. Whether or not this is true is irrelevant. What matters is that, for any cell of interest, one skilled in the art may perform assays for the involved antigens (see, for example, page 10, lines 9 to 19, of the application) and determine whether the above conjugate (or any other conjugate, for that matter) binds to such antigens. If so, the conjugate can then be used to deliver a nucleic acid to the antigen of interest on the cell of interest. This does not involve undue experimentation.

Regarding enabling the *in vivo* use of the compound, applicants refer the Examiner to Example 11 (page 46 to 49) of the application which describes the transfection of 3T3-HER2 cells using the gene delivery compounds of the present invention and comprising the following conjugates: C6ML3-9 sFv'-H1, C6ML3-9 sFv'-P1, and C6ML3-9 sFv'-SP. The transfection was conducted successfully in the presence of serum and, thus, in conditions which mimic *in vivo* conditions. It should be clear, therefore, that applicants have enabled the use of the compounds *in vivo*.

Applicants submit respectfully that the Examiner's comments respecting the nucleic acid to be bound are unclear. For example, does the Examiner consider the claims to lack enablement because he does not consider the application to provide guidance respecting which nucleic acids may be used to treat disorders on a particular cell or because he does not consider the application to provide guidance respecting which conditions must be used to ensure proper delivery and expression of the nucleic acid in the cell of interest? In considering this matter, applicants request that the Examiner consider that applicants' invention resides in the gene-delivery compound itself and in a composition comprising the compound and a nucleic acid. Applicants have fully enabled how to make such a compound (see, for example, Examples 1 to 6 of the application), how to make a composition comprising the compound and a nucleic acid (see, for example, Examples 9 to 11), and how to use the compound and composition to deliver a nucleic acid (see, for example, Examples 8 to 11).

Applicants submit that the aforementioned explanation addresses the Examiner's rejection; however, if the Examiner persists in his rejection, applicants request respectfully that he clarify the basis of his rejection. This should help in accelerating prosecution.

Discussion of the Examiner's Section 112, Second Paragraph, Rejection

It is submitted that the amendment to Claim 22 overcomes the Examiner's rejection of Claim 22 and Claim 26, which depends from Claim 22.

Conclusion

For the reasons expressed above, applicants request respectfully that the Examiner reconsider and withdraw his rejections. An early and favorable action is requested respectfully.

The Examiner is invited to telephone the undersigned to discuss matters that the Examiner believes may be relevant to placing the application in condition for allowance.

Respectfully submitted,

Gene J. Yao, Esquire
Reg. No. 47,193
Attorney for Applicants

Synnestvedt & Lechner LLP
Suite 2600 Aramark Tower
1101 Market Street
Philadelphia, PA 19107-2950
(215) 923-4466

GJY

M:\GYao\23,000 to 23,999\23,611A USA\Patent Office\Reply to 04.05.05 Action.doc